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10/618,267	07/14/2003	Jonathan Schneck	001107.00355	3951

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EXAMINER

DIBRINO, MARIANNE NMN

ART UNIT PAPER NUMBER

1644

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/618,267

Applicant(s)

SCHNECK ET AL.

Examiner

DiBrino Marianne

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-142 is/are pending in the application.
- 4a) Of the above claim(s) 16-22,30-36,42-45,51-59,63 and 66-142 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15,23-29,37-41,46-50,60-62,64 and 65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :7/14/03,2/1/04,10/5/04,12/14/05.

DETAILED ACTION

1. Applicant's response filed 7/31/06 is acknowledged and has been entered.
2. The following is in regard to Applicant's Form 1449 filed 7/14/03.

As per the Waiver of the Copy Requirement in 37 CFR 1.98 for Cited Pending U.S. Patent Applications (1287 Off. Gaz. Pat. Office 163, October 19, 2004), a copy of each cited pending U.S. patent application, or portion of the application which caused it to be listed is no longer required to be filed with an IDS if the cited application is stored in the IFW system and the cited information is limited to the specification, including the claims and drawings of the cited pending U.S. application. Accordingly, the reference application serial no. 09/642,660 cited in Applicant's Form 1449 filed 7/14/03 has been considered only as to the extent of the specification, including the claims, and drawings, and the specification, including the claims and drawings of the parent application 09/063,276 that is incorporated by reference into 09/642,660.

Applicant is reminded that if the cited information from the pending application is an Office Action, affidavit, or IDS filed in the cited pending U.S. application which is not part of the specification, a copy of the cited paper is required.

3. Applicant's election with traverse of Group I (claims 4-41 and 46-65), and species of solid support that is a bead, a T lymphocyte affecting molecule that is an antibody that specifically binds to CD28, an MHC class I complex comprising at least two fusion proteins, wherein a first fusion protein comprises a first MHC class I alpha chain and a first Ig heavy chain and wherein a second fusion protein comprises a second MHC class I alpha chain and a second Ig heavy chain, wherein the first and second Ig heavy chains associate to form the MHC class I molecular complex, wherein the MHC class I molecular complex comprises a first MHC class I peptide binding cleft and a second MHC class I peptide binding cleft in Applicant's response filed 7/31/06 is acknowledged. The basis for Applicant's traversal is that: MPEP sets forth two criteria that must be met to make a proper restriction requirement, *i.e.*, the inventions must be independent or distinct, and there must be a serious burden on the Examiner, a *prima facie* showing of a serious burden has not been met, the restriction requirement imposes a very serious burden upon Applicant in terms of cost of prosecuting and maintaining 22 separate patents, and shortening of patent term while examination of the remaining groups would be delayed.

Applicant's arguments have been fully considered, but are not persuasive.

It is the Examiner's position that regarding undue burden, the M.P.E.P. 803 (July 1998) states that: "For purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search."

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Where the related inventions as claimed are shown to be independent or distinct under the criteria of MPEP 806.05(c)-806.06, the Examiner, in order to establish reasons for insisting upon restriction, must explain why there would be a serious burden on the Examiner if restriction is not required. Thus the Examiner must show by appropriate explanation one of the following:

A. Separate classification thereof: This shows that each invention has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Patents need not be cited to show separate classification.

B. A separate status in the art when they are classifiable together: Even though they are classified together, each invention can be shown to have formed a separate subject for inventive effort when the Examiner can show a recognition of separate inventive effort by inventors. Separate status in the art may be shown by citing patents that are evidence of such separate status, and also of a separate field of search.

C. A different field of search: Where it is necessary to search for one of the inventions in a manner that is not likely to result in finding art pertinent to the other inventions (e.g., searching different classes/subclasses or electronic resources, or employing different search queries, a different field of search is shown, even though the two are classifiable together. The indicated different field of search must in fact be pertinent to the type of subject matter covered by the claims. Patents need not be cited to show different fields of search (see MPEP § 808.02).

Group I has a separate classification from Groups II-VI and IX-XXII as enunciated in the previous Office Action, and therefore, the restriction requirement set forth in the previous Office Action meets this requirement of serious burden. While Groups VII and VIII have the same classification, a different field of search is required, *i.e.*, a search for the solid support (Group I), a search for a method of immunosuppressing an immune response in a patient (Group VII), or a search for a method of upregulating an immune response in a patient (Group VIII). In addition, Applicant is reminded that Group I and each of Groups VII and VIII are related as product and process of use as enunciated in paragraphs #6 and #7 of the previous Office Action and of rejoinder practice as enunciated at paragraph #3 of the previous Office Action.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-7, 14, 23, 24, 46-50 and 64 read upon the elected species.

Upon consideration of the prior art cited in this Office Action at items # 7 and 9, the species recited in instant claims 8-13, 15, 25-29, 37-41, 60-62 and 65 are also being examined.

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Accordingly, claims 16-22, 30-36, 51-59, 63 (non-elected species of Group I) and claims 42-45 and 66-142 (non-elected groups II-XXII) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-15, 23-29, 37-41, 46-50, 60-62, 64 and 65 are currently being examined.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP, 602.01 and 602.02.

The oath or declaration is defective because: changes have been made to Inventor Oelke's P.O. address that have been initialed, but not dated.

5. The disclosure is objected to because of the following informality:

The use of the trademark GOLGISTOP has been noted in this application on page 51 at [168]. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Appropriate correction is required.

6. For the purpose of prior art rejections, the filing date of the instant claims 1-15, 23-29, 37-41, 46-50, 60-62, 64 and 65 is deemed to be the filing date of the instant application, *i.e.*, 7/14/03, as the parent application serial no. 60/395,781 does not support the claimed limitations of the instant application. Application serial no. 60/395,781 provides support for the limitations of a solid support that is a bead that has attached thereto, a co-stimulatory molecule that is an anti-CD28 antibody and an MHC class I molecule that consists of the extracellular regions of the MHC class I alpha chain as well as β 2m, and wherein the MHC class I alpha chain extracellular regions are attached at the C-terminal end to Ig constant region comprising the hinge region, and wherein the MHC class I-Ig fusion proteins form dimers. Application serial no. 60/395,781 does not provide support for the limitation "flexible solid support," nor for the limitation wherein the fusion protein "comprises at least one MHC class I peptide binding cleft" or "comprises at least one antigen binding cleft" wherein the fusion protein does not consist of the β 2m and wherein it is not part of a dimer, nor for the limitation wherein the fusion protein comprises an MHC class I alpha chain and an Ig heavy chain wherein the fusion protein comprises the entire MHC class I alpha chain and the entire Ig heavy chain, not just the extracellular regions or the Ig hinge and constant regions, respectively, and wherein the dimeric fusion proteins do not further comprise β 2m, nor for the limitation "at least one lymphocyte affecting molecule" that is not a co-stimulatory molecule or anti-CD28, nor for the T cell co-stimulatory molecules recited in instant claims 23 and 24, except for anti-CD28, nor for wherein "the at least one antigen presenting complex comprises an MHC class II peptide binding cleft" as well as the

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limitations pertaining to the MHC class II fusion proteins recited in the instant claims, nor the adhesion molecules or T cell growth factors recited in the instant claims. The said parent application does not provide support for the limitation "particle" except wherein the particle is a bead.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-6, 12-15, 23-29, 37-41 and 48-50 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2002/0122818 A1 (IDS reference in the 1449 filed 7/14/03).

US 2002/0122818 A1 discloses a solid support such as a liposome, a liposome comprising another solid support, or bead such as glass or magnetic, comprising an MHC class I complex or MHC class II complex with or without an antigenic peptide, such as from cancer-associated antigens or pathogen-associated antigens or HA peptide, and an anti-CD28 antibody. US 2002/0122818 A1 discloses that the solid support can comprise co-stimulatory, adhesion or accessory molecules such as B7-1 or B7-2 or antibody to CD40L, IL-10, IL-2, IFN- γ or IL-12 cytokines, or OX42L or CD30, or toxins that induce apoptosis or other apoptosis inducing molecules or Fas ligand. US 2002/0122818 A1 discloses use of the platform comprising the liposomes for treatment and also teaches suspending the liposomes in PBS, *i.e.*, a pharmaceutically acceptable carrier (especially [0038], [0045], [0049], [0050], [0055], [0063]-[0068], [0083]-[0085], [0110], [0113], [0018], [0119], [0120], [0122], [0181]-[0185], [0188], [0201], [0243], [0248], [0475], [0606], claims).

With regard to the inclusion of instant claim 3 in this rejection, a bead is a "particle."

9. Claims 1-9, 12-15, 27, 28, 37, 39-41, 48-50, 60-62 and 64 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,268,411 B1.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

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U.S. Patent No. 6,268,411 B1 discloses MHC class I/Ig divalent chimeric complexes or MHC class II/Ig chimeric complexes comprising four chimeric proteins, in the latter instance, wherein the MHC class II α chain is fused to the Ig heavy chain and the β chain is fused to the Ig light chain at the carboxy-terminus of the extracellular domains. U.S. Patent No. 6,268,411 B1 discloses that an identical antigenic peptide from a tumor associated antigen, a viral or infectious agent associated antigen, an autoimmune disease associated antigen, an alloantigen or xenogantigen, or an allergy associated antigen may be bound in the MHC molecule in the peptide binding groove. U.S. Patent No. 6,268,411 B1 discloses that the peptide/MHC/Ig complexes may be conjugated or fused to a toxin or a molecule such as a lymphokine or other effector molecule(s) that can stimulate an immune response and may be affixed to a solid substrate such as a glass or plastic slide or tissue culture plate or latex, PVC or polystyrene bead or a viral particle. U.S. Patent No. 6,268,411 B1 discloses that the viral particles that carry the complexes may also contain saline, a pharmaceutically acceptable carrier. U.S. Patent No. 6,268,411 B1 discloses that the MHC class I α chain is fused to the Ig heavy chain. U.S. Patent No. 6,268,411 B1 discloses that the peptide/MHC/Ig complexes can be used to stimulate T cells, and that immobilized complexes can stimulate antigen specific T cells. U.S. Patent No. 6,268,411 B1 discloses that thus, these reagents can be used to selectively activate antigen specific T cells either *in vitro* or *in vivo*. U.S. Patent No. 6,268,411 B1 discloses that the Ig heavy chain may comprise a variable region (especially abstract, Figure 1A, column 3 at lines 5-15, 30-64, column 8 at lines 9-27, column 9 at lines 24-67, column 10 at lines 12-67, column 11 at lines 1-62, column 16 at lines 55-67, claims).

10. Claims 1-4, 8-15, 39, 40, 48-50, 60-62 and 65 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,015,884 (IDS reference in the Form 1449 filed 7/14/03).

U.S. Patent No. 6,015,884 discloses MHC class II/Ig/peptide heterodimers bound with high avidity to T cells bearing their cognate receptors. U.S. Patent No. 6,015,884 discloses divalent complexes comprising the said heterodimers wherein the said complexes are comprised of at least 4 chimeric proteins, *i.e.*, the MHC class II β chain extracellular regions fused to IgG heavy chain and the MHC class II α chain extracellular regions fused to IgG light chain, and wherein the class II MHC binding sites contain an identical antigenic peptide, such as from a viral antigen, tumor antigen, alloantigen, or autoimmune antigen, and wherein the complexes may be immobilized on a substrate to stimulate antigen specific T cell responses, said substrate being a solid substrate such as a plate or bead. U.S. Patent No. 6,015,884 further discloses that the chimeric proteins may be linked or fused to a toxin or solid matrix, and may be comprised in a pharmaceutical composition with saline and optionally with cytokines such as IL-2, α IFN and IFN γ . U.S. Patent No. 6,015,884 discloses that MHC class II chimeric proteins and complexes may be constructed using heavy and light chains of Ig (especially abstract, Figure 1, summary of the invention, column 27 at lines 56-61, claims).

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Claim 11 is included in this rejection because U.S. Patent No. 6,015,884 discloses Ig heavy and light chains, *i.e.*, comprise a variable region, as well as the Fc and hinge regions of the heavy and light chains of Ig.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,268,411 B1 in view of WO 97/28191 A1 and Latouche *et al* (Nature Biotechnology. 18: 405-409, 2000, IDS reference in the Form 1449 filed 7/14/03).

U.S. Patent No. 6,268,411 B1 discloses MHC class I/Ig divalent chimeric complexes or MHC class II/Ig chimeric complexes comprising at least four fusion proteins, in the latter instance, wherein the MHC class II α chain is fused to the Ig heavy chain and the β chain is fused to the Ig light chain at the carboxy-terminus of the extracellular domains. U.S. Patent No. 6,268,411 B1 discloses that an identical antigenic peptide from a tumor associated antigen, a viral or infectious agent associated antigen, an autoimmune disease associated antigen, an alloantigen or xenogantigen, or an allergy associated antigen may be bound in the MHC molecule in the peptide binding groove. U.S. Patent No. 6,268,411 B1 discloses that the peptide/MHC/Ig complexes may be conjugated or fused to a toxin or a molecule such as a lymphokine or other effector molecule(s) that can stimulate an immune response and may be affixed to a solid substrate such as a glass or plastic slide or tissue culture plate or latex, PVC or polystyrene bead or a viral particle. U.S. Patent No. 6,268,411 B1 discloses that the viral particles that carry the complexes may also contain saline, a pharmaceutically acceptable carrier. U.S. Patent No. 6,268,411 B1 discloses that the MHC class I α chain is fused to the Ig heavy chain. U.S. Patent No. 6,268,411 B1 discloses that the peptide/MHC/Ig complexes can be used to stimulate T cells, and that immobilization of the said complexes can stimulate antigen specific T cells. U.S. Patent No. 6,268,411 B1 discloses that thus, these reagents can be used to selectively activate antigen specific T cells either *in vitro* or *in vivo*. U.S. Patent No. 6,268,411 B1 discloses that the Ig heavy chain may comprise a variable region (especially abstract, Figure 1A, column 3 at lines 5-15, 30-64, column 8 at lines 9-27, column 9 at lines 24-67, column 10 at lines 12-67, column 11 at lines 1-62, column 16 at lines 55-67, claims).

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U.S. Patent No. 6,268,411 B1 does not disclose wherein the at least one T cell affecting molecule is a T cell costimulatory molecule, including anti-CD28 antibody, wherein the at least one T cell affecting molecule is an adhesion molecule such as ICAM-1 or LFA-3, nor wherein the said molecule is IL-2, nor wherein the MHC class II β chain is fused to the Ig heavy chain and the MHC class II α chain is fused to the Ig light chain.

WO 97/28191 A1 teaches that peptide/MHC complexes on the surface of antigen presenting cells (APC) will only induce clonal expansion of a T cell line specific for the MHC bound peptide if the APC also deliver co-stimulatory signals. WO/97/28191 A1 teaches complexes of MHC class I or MHC class II molecules can be used to induce T cells, the complexes comprising the extracellular regions of the MHC molecule linked or fused to an immunoglobulin heavy and light constant region domains, and that the complexes may further comprise an antigenic peptide. WO/97/28191 A1 teaches that if DNA encoding the complexes is transfected into a cell, a co-stimulatory molecule should also be co-transfected, and that co-stimulatory molecules are B7[-1] or B7-2. WO 97/28191 A1 teaches that the α chain can be fused to the Ig light chain and the β chain can be fused to the Ig heavy chain (especially page 2 at lines 16-19, page 3 at lines 7-30, page 9 at lines 5-14, page 13 at lines 5-9, page 18 at lines 14-30, page 25 at lines 11-26, paragraph spanning pages 33-34, page 34 at lines 9-19 and lines 27-31, page 38 at lines 1-9, Figures 1B and 1C).

Latouche *et al* teach that signaling through the CD28 receptor provides a powerful costimulatory signal following engagement of the B7-1 or B7-2 ligand, and that the adhesion molecule ICAM-1 provides a synergistic signal, while LFA-3 can also mediate costimulatory as well as adhesion functions. Latouche *et al* further teach that T cells may be expanded by incubation with beads coated with anti-CD3 and anti-CD28 antibodies to engage the TCR and CD28. Latouche *et al* teach addition of IL-2 to artificial APC comprising the MHC, costimulatory and adhesion molecules when stimulating T cells (especially Introduction on page 405, paragraph spanning columns 1-2 on page 408, materials and methods section on page 409 at the first full paragraph of column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the solid support and composition thereof disclosed by U.S. Patent No. 6,268,411 B1 to also include a costimulatory molecule such as that taught by WO 97/28191 A1 to be necessary to induce clonal expansion of T cells specific for MHC/peptide complexes such as the B7-1 or B7-2 molecules taught by WO/97/28191 A1 or the anti-CD28 antibody taught by Latouche *et al*, and optionally ICAM-1 and/or LFA-3.

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One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a solid substrate comprising an MHC complex that would be effective in stimulating CD8+ T cells because both U.S. Patent No. 6,268,411 B1 and WO/97/28191 A1 teach MHC class II/Ig dimers for stimulating T cells, and both WO/97/28191 A1 and Latouche *et al* teach that signaling through the CD28 receptor either through interaction with B7-1 or B7-2 or anti-CD28 antibody provides a powerful co-stimulatory signal.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added a T cell growth factor such as IL-2 taught by Latouche *et al* to the solid support.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate T cells *in vitro* because Latouche *et al* teach addition of IL-2 to the artificial APC comprising the MHC complexes, costimulatory molecules and adhesion molecules when stimulating T cells *in vitro*.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made the MHC class II/Ig complexes as per the teaching of WO 97/28191 A1 with the α chain fused to the Ig light chain and the β chain fused to the Ig heavy chain or as disclosed by U.S. Patent No. 6,268,411 B1 with the light and heavy chains fused to β and α MHC class II chains, respectively.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO/97/28191 A1 teaches and U.S. Patent No. 6,268,411 B1 discloses that the MHC class II/Ig complexes may be constructed in either of these ways.

Claim 11 is included in this rejection because U.S. Patent No. 6,268,411 B1 discloses Ig heavy and light chains, *i.e.*, comprise a variable region, as well as the Fc and hinge regions of the heavy and light chains of Ig.

13. Claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,015,884 (IDS reference in the form 1449 filed 7/14/03) in view of WO 97/35991 A1, WO 97/28191 A1 and Latouche *et al* (Nature Biotechnology. 18: 405-409, 2000, IDS reference in the Form 1449 filed 7/14/03).

U.S. Patent No. 6,015,884 discloses MHC class II/Ig/peptide heterodimers bound with high avidity to T cells bearing their cognate receptors. U.S. Patent No. 6,015,884 discloses divalent complexes comprising the said heterodimers wherein the said complexes are comprised of at least 4 chimeric proteins, *i.e.*, the MHC class II β chain extracellular regions fused to IgG heavy chain and the MHC class II α chain extracellular regions fused to IgG light chain, and wherein the class II MHC binding sites

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contain an identical antigenic peptide, such as from a viral antigen, tumor antigen, alloantigen, or autoimmune antigen, and wherein the complexes may be immobilized on a substrate to stimulate antigen specific T cell responses, said substrate being a solid substrate such as a plate or bead. U.S. Patent No. 6,015,884 further discloses that the chimeric proteins may be linked or fused to a toxin or solid matrix, and may be comprised in a pharmaceutical composition with saline and optionally with cytokines such as IL-2, α IFN and IFN γ . U.S. Patent No. 6,015,884 discloses that MHC class II chimeric proteins and complexes may be constructed using heavy and light chains of Ig (especially abstract, Figure 1, summary of the invention, column 27 at lines 56-61, claims).

U.S. Patent No. 6,015,884 does not disclose wherein the solid support further comprises at least one T cell affecting molecule that is a co-stimulatory molecule or an adhesion molecule recited in the instant claims, nor wherein the solid support comprises an MHC class I/Ig/peptide divalent complex rather than an MHC class II/Ig/peptide complex.

WO 97/35991 A1 teaches divalent MHC class I or II molecules that are comprised of MHC class I or MHC class II extracellular regions linked or fused to Ig heavy and light chains, and further that the MHC class II divalent molecules may be immobilized on a solid substrate such as beads or tissue culture plates to stimulate antigen specific T cell responses. WO 97/35991 A1 teaches that the MHC class II divalent molecules comprise two fusion proteins that comprise an Ig heavy chain and an extracellular domain of an MHC class II β chain, and two fusion proteins that comprise an Ig light chain and an extracellular domain of an MHC class II α chain. WO 97/35991 A1 teaches that the Ig heavy or light chain may comprise a variable region sequence (especially abstract, page 8 at lines 3-28, paragraph spanning pages 9-10, page 15 at lines 21-22, page 20 at lines 3-12, page 23 at lines 13-27, Figure 1).

WO 97/28191 A1 teaches that peptide/MHC complexes on the surface of antigen presenting cells (APC) will only induce clonal expansion of a T cell line specific for the MHC bound peptide if the APC also deliver co-stimulatory signals. WO/97/28191 A1 teaches complexes of MHC class I or MHC class II molecules can be used to induce T cells, the complexes comprising the extracellular regions of the MHC molecule linked or fused to an immunoglobulin heavy and light constant region domains, and that the complexes may further comprise an antigenic peptide. WO 97/28191 A1 teaches that if DNA encoding the complexes is transfected into a cell, a co-stimulatory molecule should also be co-transfected, and that co-stimulatory molecules are B7[-1] or B7-2. WO 97/28191 A1 teaches that the α chain can be fused to the Ig light chain and the β chain can be fused to the Ig heavy chain (especially page 2 at lines 16-19, page 3 at lines 7-30, page 9 at lines 5-14, page 13 at lines 5-9, page 18 at lines 14-30, page 25 at lines 11-26, paragraph spanning pages 33-34, page 34 at lines 9-19 and lines 27-31, page 38 at lines 1-9, Figures 1B and 1C).

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Latouche *et al* teach that signaling through the CD28 receptor provides a powerful costimulatory signal following engagement of the B7-1 or B7-2 ligand, and that the adhesion molecule ICAM-1 provides a synergistic signal, while LFA-3 can also mediate costimulatory as well as adhesion functions. Latouche *et al* further teach that T cells may be expanded by incubation with beads coated with anti-CD3 and anti-CD28 antibodies to engage the TCR and CD28. Latouche *et al* teach addition of IL-2 to artificial APC comprising the MHC, costimulatory and adhesion molecules when stimulating T cells (especially Introduction on page 405, paragraph spanning columns 1-2 on page 408, materials and methods section on page 409 at the first full paragraph of column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the solid support disclosed by U.S. Patent No. 6,015,884 to have also included a costimulatory molecule such as that taught by WO 97/28191 A1 to be necessary to induce clonal expansion of T cells specific for MHC/peptide complexes such as the B7-1 or B7-2 molecules taught by WO/97/28191 A1 or the anti-CD28 antibody taught by Latouche *et al*, and optionally the adhesion molecule(s) ICAM-1 and/or LFA-3.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a solid substrate comprising an MHC complex that would be effective in stimulating CD8+ T cells because both U.S. Patent No. 6,015,884 and WO 97/28191 A1 teach MHC class II dimers for stimulating T cells, and both WO 97/28191 A1 and Latouche *et al* teach that signaling through the CD28 receptor either through interaction with B7-1 or B7-2 or anti-CD28 antibody provides a powerful co-stimulatory signal and WO 97/35991 A1 teaches immobilizing the MHC/II complexes on a solid support.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added a T cell growth factor such as IL-2 taught by Latouche *et al* or as disclosed by U.S. Patent No. 6,015,884 to the solid support.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate T cells *in vitro* because Latouche *et al* teach and U.S. Patent No. 6,015,884 discloses addition of IL-2 to compositions comprising the MHC complexes when stimulating T cells *in vitro*.

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14. Claims 1-15, 23-29, 37, 41, 46-50, 60-62, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/35991 A1 in view of WO 97/28191 A1 and Latouche *et al* (Nature Biotechnology. 18: 405-409, 2000, IDS reference in the Form 1449 filed 7/14/03).

WO 97/35991 A1 teaches divalent MHC class I or II molecules that are comprised of MHC class I or MHC class II extracellular regions linked or fused to Ig heavy and light chains, and further that the MHC class II divalent molecules may be immobilized on a solid substrate such as beads or tissue culture plates to stimulate antigen specific T cell responses. WO 97/35991 A1 teaches that the MHC class II divalent molecules comprise two fusion proteins that comprise an Ig heavy chain and an extracellular domain of an MHC class II β chain, and two fusion proteins that comprise an Ig light chain and an extracellular domain of an MHC class II α chain. WO 97/35991 A1 teaches that the Ig heavy or light chain may comprise a variable region sequence (especially abstract, page 8 at lines 3-28, paragraph spanning pages 9-10, page 15 at lines 21-22, page 20 at lines 3-12, page 23 at lines 13-27, Figure 1).

WO 97/35991 A1 does not teach wherein the divalent MHC class I molecules are attached to a solid support and wherein the solid support further comprises at least one lymphocyte affecting molecule that is a co-stimulatory molecule.

WO 97/28191 A1 teaches that peptide/MHC complexes on the surface of antigen presenting cells (APC) will only induce clonal expansion of a T cell-line specific for the MHC bound peptide if the APC also deliver co-stimulatory signals. WO 97/28191 A1 teaches complexes of MHC class I or MHC class II molecules can be used to induce T cells, the complexes comprising the extracellular regions of the MHC molecule linked or fused to an immunoglobulin heavy and light constant region domains, and that the complexes may further comprise an antigenic peptide. WO 97/28191 A1 teaches that if DNA encoding the complexes is transfected into a cell, a co-stimulatory molecule should also be co-transfected, and that co-stimulatory molecules are B7[-1] or B7-2. WO 97/28191 A1 teaches linkage of an antigenic peptide to the divalent class II MHC molecules, said antigenic peptide derived from moth cytochrome C amino acid residues 81-101 for stimulating T cells, and that T cells respond to peptide antigen in the context of either class I or class II MHC molecules, said peptide antigens being from viral or tumor or transplantation antigens, said peptide antigens binding in the antigen binding site of MHC molecules. WO 97/28191 A1 teaches formulation of the said complexes in a pharmaceutically acceptable carrier such as saline (especially page 2 at lines 16-19, page 3 at lines 7-30, page 9 at lines 5-14, page 13 at lines 5-9, page 18 at lines 14-30, page 25 at lines 11-26, paragraph spanning pages 33-34, page 34 at lines 9-19 and lines 27-31, page 38 at lines 1-9, Figures 1B and 1C).

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Latouche *et al* teach that signaling through the CD28 receptor provides a powerful costimulatory signal following engagement of the B7-1 or B7-2 ligand, and that the adhesion molecule ICAM-1 provides a synergistic signal, while LFA-3 can also mediate costimulatory as well as adhesion functions. Latouche *et al* further teach that T cells may be expanded by incubation with beads coated with anti-CD3 and anti-CD28 antibodies to engage the TCR and CD28. Latouche *et al* teach addition of IL-2 to compositions comprising the MHC complexes when stimulating T cells *in vitro*. (especially Introduction on page 405, paragraph spanning columns 1-2 on page 408, materials and methods on page 409, column 1, first full paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have immobilized the MHC class I/Ig fusion dimers taught by WO 97/35991 A1 and by WO 97/28191 A1 on a solid support as taught for the MHC class II/Ig fusion dimers taught by WO 97/35991 A1, and to have also immobilized a costimulatory molecule such as taught by WO 97/28191 A1 to be necessary to induce clonal expansion of T cells specific for MHC/peptide complexes such as the B7-1 or B7-2 molecules taught by WO 97/28191 A1 or the anti-CD28 antibody taught by Latouche *et al*, and optionally ICAM-1 and/or LFA-3, and further to have loaded the MHC/Ig fusion dimers with antigenic peptide as taught by WO 97/28191 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a solid substrate comprising an MHC complex that would be effective in stimulating CD8+ T cells because both WO 97/35991 A1 and by WO 97/28191 A1 teach MHC class I/Ig dimers for stimulating CD8+ T cells, WO 97/35991 A1 teaches that MHC/Ig dimers may be immobilized on a solid substrate such as a bead for stimulating T cells, both WO 97/28191 A1 and Latouche *et al* teach that signaling through the CD28 receptor either through interaction with B7-1 or B7-2 or anti-CD28 antibody provides a powerful co-stimulatory signal.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have formulated the beads comprising the fusion dimers and other molecules in saline such as taught by WO 97/28191 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to store the beads in a compatible buffered solution because saline or PBS is taught by WO 97/28191 A1 to be compatible with the protein component and is a commonly available carrier as was known to one of ordinary skill in the art at the time the invention was made.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added a T cell growth factor such as IL-2 taught by Latouche *et al* to the solid support.

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One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate T cells *in vitro* because Latouche *et al* teach addition of IL-2 to compositions comprising the MHC complexes when stimulating T cells *in vitro*.

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-104 of U.S. Patent No. 6,268,411 B1 (IDS reference in the Form 1449 filed 7/14/03) in view of in view of WO 97/35991 A1, WO 97/28191 A1 and Latouche *et al* (Nature Biotechnology. 18: 405-409, 2000, IDS reference in the Form 1449 filed 7/14/03).

Instant claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are drawn to a solid support comprising a least one lymphocyte affecting molecule and at least one molecular complex that when bound to an antigen engages a unique clonotypic receptor, wherein the said complex comprises at least two MHC class I or at least four MHC class II/Ig fusion proteins.

Claims 1-104 of U.S. Patent No. 6,268,411 B1 are drawn to a composition comprising at least two chimeric proteins, wherein each chimeric protein comprises an MHC molecule and an Ig chain.

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Claims 1-104 of U.S. Patent No. 6,268,411 B1 do not recite wherein the said composition is linked to a solid support.

The complexes recited in claims 1-104 of U.S. Patent No. 6,268,411 B1 are encompassed by the complexes of the solid support recited in the instant claims.

WO 97/35991 A1 teaches divalent MHC class I or II molecules that are comprised of MHC class I or MHC class II extracellular regions linked or fused to Ig heavy and light chains, and further that the MHC class II divalent molecules may be immobilized on a solid substrate such as beads or tissue culture plates to stimulate antigen specific T cell responses. WO 97/35991 A1 teaches that the MHC class II divalent molecules comprise two fusion proteins that comprise an Ig heavy chain and an extracellular domain of an MHC class II β chain, and two fusion proteins that comprise an Ig light chain and an extracellular domain of an MHC class II α chain. WO 97/35991 A1 teaches that the Ig heavy or light chain may comprise a variable region sequence (especially abstract, page 8 at lines 3-28, paragraph spanning pages 9-10, page 15 at lines 21-22, page 20 at lines 3-12, page 23 at lines 13-27, Figure 1).

WO 97/28191 A1 teaches that peptide/MHC complexes on the surface of antigen presenting cells (APC) will only induce clonal expansion of a T cell line specific for the MHC bound peptide if the APC also deliver co-stimulatory signals. WO/97/28191 A1 teaches complexes of MHC class I or MHC class II molecules can be used to induce T cells, the complexes comprising the extracellular regions of the MHC molecule linked or fused to an immunoglobulin heavy and light constant region domains, and that the complexes may further comprise an antigenic peptide. WO 97/28191 A1 teaches that if DNA encoding the complexes is transfected into a cell, a co-stimulatory molecule should also be co-transfected, and that co-stimulatory molecules are B7[-1] or B7-2. WO 97/28191 A1 teaches that the α chain can be fused to the Ig light chain and the β chain can be fused to the Ig heavy chain (especially page 2 at lines 16-19, page 3 at lines 7-30, page 9 at lines 5-14, page 13 at lines 5-9, page 18 at lines 14-30, page 25 at lines 11-26, paragraph spanning pages 33-34, page 34 at lines 9-19 and lines 27-31, page 38 at lines 1-9, Figures 1B and 1C).

Latouche *et al* teach that signaling through the CD28 receptor provides a powerful costimulatory signal following engagement of the B7-1 or B7-2 ligand, and that the adhesion molecule ICAM-1 provides a synergistic signal, while LFA-3 can also mediate costimulatory as well as adhesion functions. Latouche *et al* further teach that T cells may be expanded by incubation with beads coated with anti-CD3 and anti-CD28 antibodies to engage the TCR and CD28. Latouche *et al* teach addition of IL-2 to artificial APC comprising the MHC, costimulatory and adhesion molecules when stimulating T cells (especially Introduction on page 405, paragraph spanning columns 1-2 on page 408, materials and methods section on page 409 at the first full paragraph of column 1).

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It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the complexes and composition thereof recited in the claims of U.S. Patent No. 6,268,411 B1 to immobilize the said complexes on a solid support as taught by WO 97/35991 A1 for the MHC/Ig divalent complexes and to have also included a costimulatory molecule such as that taught by WO/97/28191 A1 to be necessary to induce clonal expansion of T cells specific for MHC/peptide complexes such as the B7-1 or B7-2 molecules taught by WO/97/28191 A1 or the anti-CD28 antibody taught by Latouche *et al*, and optionally ICAM-1 and/or LFA-3.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a solid substrate comprising an MHC complex that would be effective in stimulating CD8+ T cells because both the claims of U.S. Patent No. 6,268,411 B1 recite and WO 97/28191 A1 teach MHC class /Ig dimers for stimulating T cells, and both WO 97/28191 A1 and Latouche *et al* teach that signaling through the CD28 receptor either through interaction with B7-1 or B7-2 or anti-CD28 antibody provides a powerful co-stimulatory signal, and WO 97/35991 A1 teaches immobilizing the MHC/Ig complexes on a solid support.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added a T cell growth factor such as IL-2 taught by Latouche *et al* to the solid support.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate T cells *in vitro* because Latouche *et al* teach addition of IL-2 to the artificial APC comprising the MHC complexes, costimulatory molecules and adhesion molecules when stimulating T cells *in vitro*.

17. Claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are directed to an invention not patentably distinct from claims 1-104 of commonly assigned U.S. Patent No. 6,268,411 B1 in view of in view of WO 97/35991 A1, WO/97/28191 A1 and Latouche *et al* (Nature Biotechnology. 18: 405-409, 2000, IDS reference in the Form 1449 filed 7/14/03) as enunciated above at item #16 of this Office Action.

18. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,268,411 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

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A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

19. Claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 4-10 of U.S. Patent No. 6,015,884 in view of in view of WO 97/35991 A1, WO 97/28191 A1 and Latouche *et al* (Nature Biotechnology. 18: 405-409, 2000, IDS reference in the Form 1449 filed 7/14/03).

Instant claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are drawn to a solid support comprising a least one lymphocyte affecting molecule and at least one molecular complex that when bound to an antigen engages a unique clotypic receptor, wherein the said complex comprises at least two MHC class I or at least four MHC class II/Ig fusion proteins.

Claims 1, 2 and 4-10 of U.S. Patent No. 6,015,884 are drawn to a molecular complex which comprises at least four fusion proteins, including wherein each chimeric protein comprises an MHC class II molecule α or β chain fused to an Ig chain.

Claims 1, 2 and 4-10 of U.S. Patent No. 6,015,884 do not recite wherein the said complex is linked to a solid support, nor wherein the solid support further comprises at least one lymphocyte affecting molecule as recited in the instant claims.

WO 97/35991 A1 teaches divalent MHC class I or II molecules that are comprised of MHC class I or MHC class II extracellular regions linked or fused to Ig heavy and light chains, and further that the MHC class II divalent molecules may be immobilized on a solid substrate such as beads or tissue culture plates to stimulate antigen specific T cell responses. WO 97/35991 A1 teaches that the MHC class II divalent molecules comprise two fusion proteins that comprise an Ig heavy chain and an extracellular domain of an MHC class II β chain, and two fusion proteins that comprise an Ig light chain and an extracellular domain of an MHC class II α chain. WO 97/35991 A1 teaches that the Ig heavy or light chain may comprise a variable region sequence (especially abstract, page 8 at lines 3-28, paragraph spanning pages 9-10, page 15 at lines 21-22, page 20 at lines 3-12, page 23 at lines 13-27, Figure 1).

WO 97/28191 A1 teaches that peptide/MHC complexes on the surface of antigen presenting cells (APC) will only induce clonal expansion of a T cell line specific for the MHC bound peptide if the APC also deliver co-stimulatory signals. WO/97/28191 A1 teaches complexes of MHC class I or MHC class II molecules can be used to induce T cells, the complexes comprising the extracellular regions of the MHC molecule linked or fused to an immunoglobulin heavy and light constant region domains, and that the complexes may further comprise an antigenic peptide. WO 97/28191 A1 teaches that if

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DNA encoding the complexes is transfected into a cell, a co-stimulatory molecule should also be co-transfected, and that co-stimulatory molecules are B7[-1] or B7-2. WO 97/28191 A1 teaches that the α chain can be fused to the Ig light chain and the β chain can be fused to the Ig heavy chain (especially page 2 at lines 16-19, page 3 at lines 7-30, page 9 at lines 5-14, page 13 at lines 5-9, page 18 at lines 14-30, page 25 at lines 11-26, paragraph spanning pages 33-34, page 34 at lines 9-19 and lines 27-31, page 38 at lines 1-9, Figures 1B and 1C).

Latouche *et al* teach that signaling through the CD28 receptor provides a powerful costimulatory signal following engagement of the B7-1 or B7-2 ligand, and that the adhesion molecule ICAM-1 provides a synergistic signal, while LFA-3 can also mediate costimulatory as well as adhesion functions. Latouche *et al* further teach that T cells may be expanded by incubation with beads coated with anti-CD3 and anti-CD28 antibodies to engage the TCR and CD28. Latouche *et al* teach addition of IL-2 to artificial APC comprising the MHC, costimulatory and adhesion molecules when stimulating T cells (especially Introduction on page 405, paragraph spanning columns 1-2 on page 408, materials and methods section on page 409 at the first full paragraph of column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the complexes recited in the claims of U.S. Patent No. 6,015,884 to immobilize the said complexes on a solid support as taught by WO 97/35991 A1 for the MHC/Ig divalent complexes and to have also included a costimulatory molecule such as that taught by WO 97/28191 A1 to be necessary to induce clonal expansion of T cells specific for MHC/peptide complexes such as the B7-1 or B7-2 molecules taught by WO/97/28191 A1 or the anti-CD28 antibody taught by Latouche *et al*, and optionally ICAM-1 and/or LFA-3.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a solid substrate comprising an MHC complex that would be effective in stimulating CD8+ T cells because the claims of U.S. Patent No. 6,015,884 recite and WO 97/28191 A1 teach MHC class II/Ig dimers for stimulating T cells, and both WO 97/28191 A1 and Latouche *et al* teach that signaling through the CD28 receptor either through interaction with B7-1 or B7-2 or anti-CD28 antibody provides a powerful co-stimulatory signal, and WO 97/35991 A1 teaches immobilizing the MHC/Ig complexes on a solid support.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have added a T cell growth factor such as IL-2 taught by Latouche *et al* to the solid support.

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One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate T cells *in vitro* because Latouche *et al* teach addition of IL-2 to the artificial APC comprising the MHC complexes, costimulatory molecules and adhesion molecules when stimulating T cells *in vitro*.

20. Claims 1-15, 23-29, 37, 39-41, 46-50, 60-62, 64 and 65 are directed to an invention not patentably distinct from claims 1, 2 and 4-10 of commonly assigned U.S. Patent No. 6,015,884 in view of in view of WO 97/35991 A1, WO/97/28191 A1 and Latouche *et al* (Nature Biotechnology. 18: 405-409, 2000, IDS reference in the Form 1449 filed 7/14/03) as enunciated above at item #19 of this Office Action.

21. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,015,884, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

22. No claim is allowed.

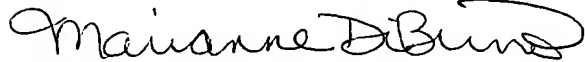
23. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware of in the specification.

24. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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